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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,220	10/01/2004	Jose Ignacio Andres-Gil	JAB-1690	6227

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EXAMINER

BERNHARDT, EMILY B

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/510,220

Applicant(s)

ANDRES-GIL ET AL.

Examiner

Emily Bernhardt

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 10/01/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

PTO records along with applicants' oath indicate that 119 benefit is being claimed yet the BIB Data sheet does not show the foreign priority document.

Applicants should request a corrected filing receipt.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. "Oxo" as a substituent for "Ar" rings makes no sense since valency requirements for carbon in the aromatic rings would be exceeded.
2. Nature of optional substituents for rings and chains in the R3 definition is of indeterminate scope since there is no clear definition of what is intended other than the preferred embodiments recited in claim 3. Also it's not clear if the N, O and S atoms recited are referring to the chains or rings.
3. Claim 7 does not further limit the scope of preceding claims since intended uses in such claims are given no material weight. The claim should be cancelled.
4. Claim 8 is of unknown scope. Specification provides no guidance as to what type of precursor compound would provide instant compounds in any *in vivo* environment. Metabolites for instance would be expected to have differing degradation pathways in different species based on the enzymes present and for prodrugs, one would need to know the nature of the desired pharmacokinetic effect in

designing suitable prodrug(s). No such properties are ever described in the instant disclosure.

5. "Dioxyl" as a monovalent "Het" ring is of unknown scope as this is not an art-recognized moiety. The same applies to "dioxolyl"

6. Claim 18 is an independent claim and thus needs to be complete as written. Thus all the variables recited therein must be defined therein and not referred back to final products claimed in claim 1.

Claim 8 is also objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims recites subject matter outside the scope of claims from which it depends as degraded products are not included in claim 1.

Claims 9-11,14,18 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot refer back to different sets of claims to different features. See MPEP § 608.01(n).

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11 and 13-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims drafted in terms of "use" have been held to be nonstatutory. Note *Clinical products v. Brenner* 149 USPQ 475. Accordingly, said claims will not be treated further on the merits until they are amended to statutory form.

Claims 1-5,7-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. 1. Starting material sources for the tetracyclic rings resulting from the joining of R1/R2 are not seen but are required. Specification is silent as to the availability of necessary reactants needed to prepare such ring systems of if they are commercially available. Only ring system made corresponds to that embraced in claim 6 when X=O. Note *In re Howarth* 210 USPQ 689; *Ex parte Moersch* 104 USPQ 122 for the need to show starting material sources commensurate with the claims' scope.

2. As there are no such other polycyclic compounds that have been made

corresponding to the instant scope which includes oxazolo-fused, imidazolo-fused, pyrazino fused with varying X choices, there is no reasonable basis for assuming that the myriad of compounds embraced by the all the generic claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. The same applies for the scope of "Het" substituents permitted in R10/R11 which includes heteroaryls as well as saturated rings of a wide diversity both directly and indirectly attached to the benzene ring and further substituted with more groups. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art.

Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the millions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature as it involves binding to adrenergic (α_2) receptors and serotonin reuptake inhibitory activity. It is well established that "the scope of enablement varies

inversely with the degree of unpredictability of the factors involved” and physiological activity is generally considered to be unpredictable. See *In re Fisher* 166 USPQ 18. A range for pIC₅₀ values is reported which is enormous- covering 10⁻⁶ to 10⁻⁹ M fold spread;

3) Direction or guidance- as stated above the compounds made are not representative of the instant scope but when fused at R1/R2 are directed to the core covered in claim 6 and when NR10R11 is present, “Het” rings made are either pyridinyl, pyrrolidinyl or morpholino;

4) State of the prior art- The compounds are fused isoxazoline derivatives with mandatory substitution on the benzene ring with NR10R11 or further fusion thereon. While such compounds having the basic skeleton are known as evidenced by commonly assigned WO’484, cited by applicants, it does not evidence the structural permutations required within the instant scope are known for at least one use in the prior art;


5) Working examples- While actual test data has been presented , a wide range has been reported and thus it is clear that the nature of substituents on the basic core is also responsible for activity and raises the question out of the many groups pointed out above that have not been tested , might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

Commonly assigned 10/468555 which corresponds to WO'484, lacks either the NR10R11 group or the particular fusion at R1/R2- either of which must be present in the instant compounds. WO'317 cited in applicants' search report has "Pir"rings directly attached to the isoxazole system and is fully unsaturated in the azole ring.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.


Emily Bernhardt
Primary Examiner
Art Unit 1624